

**REMARKS****Status of Claims**

Claims 1-24 are pending after entry of this paper. Claims 14-24 have been rejected. Claims 1-13 have been previously withdrawn. Claims 25 and 26 have been added. Applicants reserve the right to pursue withdrawn claims in a divisional or continuing application.

New claims 25 and 26 have been added. The support for the newly added claims may be found throughout the instant specification, for instance, paragraph [0046] of the specification as published.

No new matter has been introduced by these amendments. Reconsideration and withdrawal of the pending rejections in view of the above claim amendments and below remarks are respectfully requested.

**Withdrawn Rejections**

Applicants acknowledge that the rejection to claims 14-17 and 19-24 under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 5,688,642 to Chrisey in view of U.S. Patent Publication No. 2002/0039742 to Iwaki and in further view of U.S. Patent Publication No. 2002/0198314 to Meisenburg has been withdrawn in view of the arguments presented in the response filed on July 1, 2008.

Applicants also acknowledge that the rejection to claims 14 and 18 under 35 U.S.C. §103(a) as allegedly being unpatentable over Chrisey in view of Iwaki, and further in view of U.S. Patent No. 5,688,642 to McGovern has been withdrawn in view of the arguments presented in the response filed on July 1, 2008.

Response to Rejections under 35 U.S.C. §103

Claims 14-16 and 19-24 have been rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent Publication No. 2002/0110903 to Iwaki in view of U.S. Patent No. 5,858,653 to Duran. The Examiner contends that Iwaki teaches a method of immobilizing a probe on a solid phase carrier that allegedly includes the steps of providing a probe molecules having an ionic group such as a mercapto group, thus allegedly teaching a probe having a first functional group. The Examiner also contends that Iwaki teaches an immobilization substrate having a second functional group comprising an amino group and the interaction between two functional group is through “electrostatic bonding, i.e., without covalent bonding” (Office Action – page 4). The Examiner concludes that “[t]eachings of Iwaki et al of first functional mercapto group on the oligonucleotide and second functional amino group on the substrate and formation of ionic bond between the probe and substrate implicitly encompasses two functional groups are directly bonded through ionic bonds.” (Office Action – page 4). While, the Examiner admits that Iwaki is silent about the direct bonding between mercapto and amino functional groups via ionic bond (Office Action – page 4), the Examiner contends that it is allegedly made obvious by Duran (Office Action – page 6). Applicants respectfully disagree.

Contrary to the Examiner’s contention, the combination of prior art references does not teach each and every element of the claimed invention, either explicitly or inherently, as presented in the independent claims 14 and 24. The Examiner attempts to reach the claimed method by pointing to paragraphs [0009] and [0023] of Iwaki for the disclosure of the mercapto group as the first functional group and to Figure 2 (paras. [0058]-[0059]) of Iwaki for the disclosure of the amino-group as the second functional group.

Paragraph [0009] of Iwaki (“BACKGROUND OF THE INVENTION”) teaches the binding of a DNA oligomer with a substituted mercapto group to a silane with either exposed functional amino, aldehyde or epoxy group. Paragraph [0009] of Iwaki explicitly states that the fixation of the oligonucleotide occurs by the covalent bonding, *e.g.*, covalent bonding between mercapto and amino groups. Applicants respectfully wish to remind the Examiner that “[a] prior art reference must be considered in its entirety... including portions that would lead away from the claimed invention” (MPEP 2141). In fact, the disclosure in paragraph [0009] of Iwaki would clearly lead away from the claimed invention, because the synthesized oligonucleotide probe with a mercapto group and the surface of the solid carrier with an amino group are explicitly disclosed by Iwaki to be used in covalent bond formation, whereas the claimed invention is directed to a coupling without any covalent bonding. In fact, the covalent bonding is desirable according to Iwaki, because it produces bonding which is highly stable as compared with the electrostatic bonding. Contrary to the Examiner’s contention, paragraph [0009] of Iwaki does not support the notion that the mercapto group can be used as the first functional group in the ionic (electrostatic) bond formation.

Paragraph [0023] of Iwaki on the other hand discloses that “[t]he ionic reactive groups are amino groups or mercapto groups.” Applicants respectfully direct the Examiner’s attention to the fact that Iwaki also teaches that the ionic reactive groups are fixed on the detection device by covalent bonding (see para. [0031]) as indicated in Figure 2 by X<sup>+</sup> and para. [0059] cited by the Examiner. Thus, in fact, Iwaki teaches that the mercapto group should be used as a second functional group fixed on the immobilization substrate and not, as alleged by the Examiner, as the first functional group attached to the probe for the electrostatic interaction. A skilled artisan could not and would consider such clear and explicit disclosure of mercapto

group as either covalent bonding partner or as the second functional group attached to the solid support as an implicit disclosure of the mercapto group that can be used as the first functional group attached to the probe other than for the covalent bonding disclosed in paragraph [0009] of Iwaki.

Furthermore, while the Examiner admits that Iwaki is silent about the direct bonding between mercapto and amino functional groups via ionic bond (Office Action – page 4), the Examiner looks to Duran and contends that the direct bonding between mercapto group and amino group via ionic bond was known in the art as taught by Duran (Office Action – page 7). To support this notion, the Examiner points to Column 3, lines 21-33 of Duran.

If this is the Examiner's position, it appears that the Examiner misunderstood the disclosure of Duran. Once again, applicants respectfully wish to remind the Examiner that "[a] prior art reference must be considered in its entirety... including portions that would lead away from the claimed invention" (MPEP 2141). Applicants respectfully assert that Column 3, lines 21-33 of Duran does not support the direct bonding between mercapto group and amino group via ionic bond as suggested by the Examiner. Duran teaches a system (reagent composition) composed of 1) photogroups, 2) reactive groups, and 3) attractive groups that allows a target molecule to be fixed on the surface of a substrate. The section of the Duran (Column 3, lines 21-33) cited by the Examiner teaches the presence of ionic groups, e.g., cationic groups such as quaternary ammonium groups or protonated (i.e., acidified) tertiary amines, that serve to attract the nucleic acid sequence to the surface by means of electrostatic and other forces. This attraction, in turn, enhances the ability of the reactive groups<sup>1</sup> to efficiently couple with corresponding reactive groups on the nucleic acid sequence. (see Col. 3, lines 25-28). The

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<sup>1</sup> Duran defines reactive groups as groups that form covalent bonds; see Col. 3, lines 5-8

corresponding reactive groups on the nucleic acid sequence, Duran teaches, can be amine and/or sulfhydryl groups that forms covalent bonds with corresponding functional groups on the surface of the substrate. For support, for instance, see claim 21 of Duran that states:

A method for attaching a target molecule to the surface of a substrate, the method comprising the steps of

(a) providing upon the surface of the substrate a reagent composition comprising one or more groups for attracting the target molecule to the reagent composition, and **one or more thermochemically amine-reactive or sulfhydryl-reactive groups for forming covalent bonds with corresponding functional groups** on the attracted target molecule,

(b) bringing the target molecule into sufficient proximity to the surface to permit the attractive groups to attract the target molecule to the bound reagent composition, and

(c) allowing the thermochemically reactive groups to form covalent bonds with the attracted target molecule.

Thus, contrary to the Examiner's contention, Duran does not teach the direct bonding between mercapto group and amino group via ionic bond. Duran suggests either mercapto (sulfhydryl) or amine group as possible reactive groups that can form a covalent bond between the substrate and the target when the target molecule is attracted to the substrate through ionic interactions between the cationic groups (attractive groups) on the substrate and the negatively charged phosphodiester groups on the oligonucleotide (Column 3, lines 21-33). The section cited by the Examiner (Office Action – pages 6-7) must be read carefully to differentiate between two separate systems: 1) attractive groups, for instance, protonated tertiary amines and the phosphate backbone of the oligonucleotide that form electrostatic bonding, and 2) the reactive groups such as amine and sulfhydryl groups that form covalent bond. The Examiner has improperly combined two systems to allege that Duran teaches the direct bonding between mercapto group and amino group via ionic bond.

In light of the above arguments, the applicants assert that neither Iwaki, nor Duran alone, or the combination thereof satisfy all of the elements of the claimed method. Duran does not remedy the deficiencies in the method described by Iwaki, and in fact both Iwaki and Duran teach away from using the mercapto group with the amino group to form non-covalent ionic bond (see para. [0009] of Iwaki and claim 21 of Duran). Therefore, the combination of Iwaki and Duran does not make obvious the claimed invention. The applicants respectfully request reconsideration and withdrawal of the 35 U.S.C. §103(a) rejection of claims 14-16 and 19-24 in view of the aforementioned remarks and amendments to the claims.

Claims 14, 16, 17, and 18 have been rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over U.S. Patent Publication No. 2002/0110903 to Iwaki in view of U.S. Patent No. 5,858,653 to Duran, as applied to claim 14, and further in view of U.S. Patent No. 6,159,695 to McGovern. Applicants respectfully disagree.

Claim 14 is directed to a method of immobilizing a probe that is specifically bindable to a target substance. As demonstrated above, the combination of Iwaki and Duran does not teach each and every element of the claimed invention as disclosed in claim 14. The McGovern reference, on the other hand, does not compensate for the shortcomings of Iwaki and Duran.

Applicants assert that the combination of Iwaki, Duran, and McGovern does not teach, disclose, or suggest the method claimed in claim 17. Specifically, applicants respectfully assert that McGovern does not cure the deficiencies of Iwaki and Duran noted in the previous subsection. Thus, applicants contend, that the proposed combination of references fails to teach, disclose, or suggest all of the claim elements of applicant's invention. For at least these reasons,

reconsideration and withdrawal of the rejections of the claims 14, 16, 17, and 18 are respectfully requested.

#### Dependent Claims

The applicants have not independently addressed all of the rejections of the dependent claims. The applicants submit that for at least similar reasons as to why independent claims 14 and 24 from which all of the dependent claims 15-23 depend are believed allowable as discussed *supra*, the dependent claims are also allowable. The applicants however, reserve the right to address any individual rejections of the dependent claims and present independent bases for allowance for the dependent claims should such be necessary or appropriate.

Thus, applicants respectfully submit that the invention as recited in the claims as presented herein is allowable over the art of record, and respectfully request that the respective rejections be withdrawn.

Based on the foregoing remarks and arguments, the applicants respectfully request reconsideration and withdrawal of the pending rejections and allowance of this application. The applicants respectfully submit that the instant application is in condition for allowance. Entry of the arguments presented herein and an action passing this case to issue is therefore respectfully requested. In the event that a telephone conference would facilitate examination of this application in any way, the Examiner is invited to contact the undersigned at the number provided. Favorable action by the Examiner is earnestly solicited.

**AUTHORIZATION**

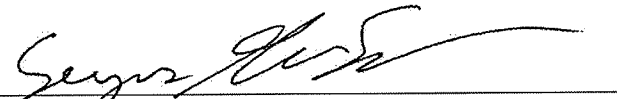
The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. **13-4500**, Order No. 1232-5579.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. **13-4500**, Order No. 1232-5579.

Respectfully submitted,  
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